I microRNA circolanti come biomarcatori della fisiologia dell'astronauta, lo studio degli effetti delle condizioni ambientali spaziali, prevenzione e diagnosi di patologie

## **Andrea Masotti**

Laboratori di Ricerca, Ospedale Pediatrico Bambino Gesù - Roma



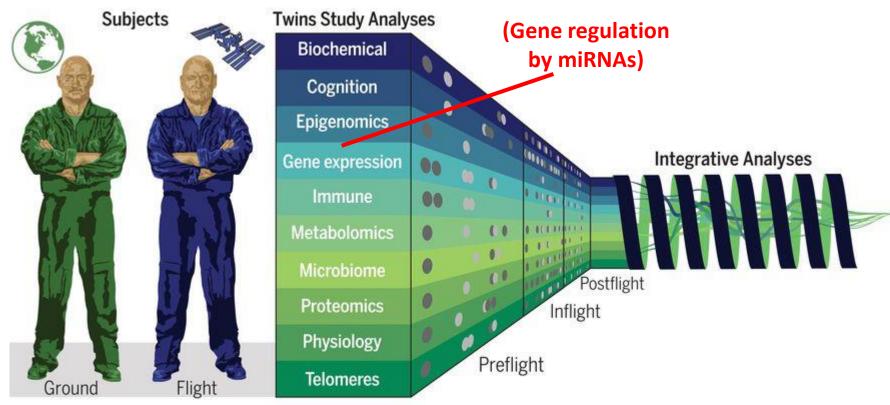




# The NASA Twins Study

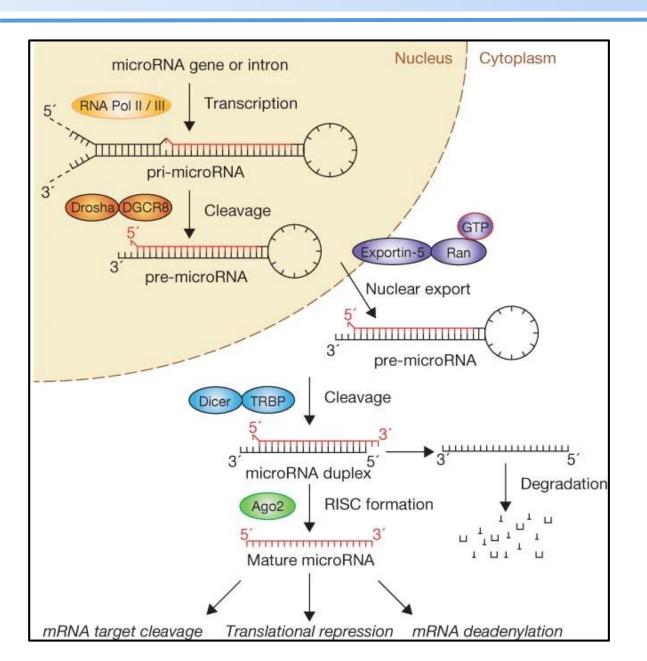


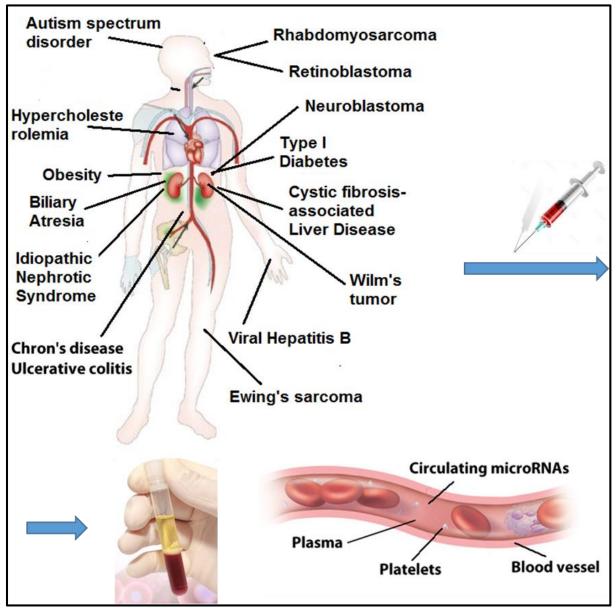
The identical *twin* astronauts
Scott and Mark Kelly



Garrett-Bakelman FE, et al. The NASA Twins Study: A multidimensional analysis of a year-long human spaceflight. Science. 2019 Apr 12;364(6436):eaau8650.

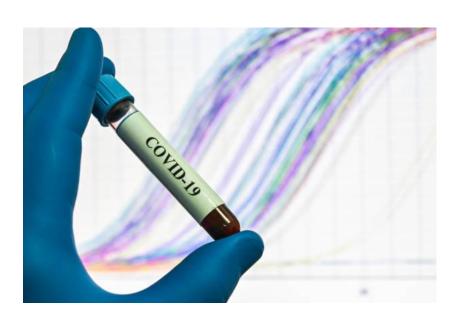
## The microRNA world

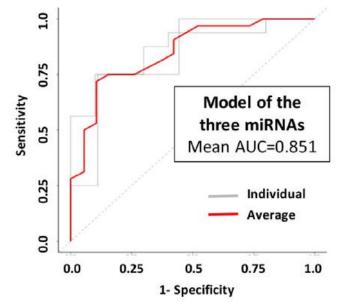




# "Liquid biopsies" (i.e., Exosomes, cDNA, cRNA, etc.)









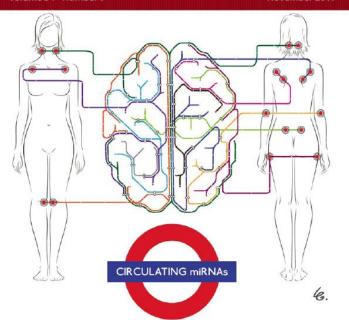
# Fibromialgia and Insulin resistance in Obese patients

Circulating microRNA Profiles as Liquid Biopsies for the Characterization and Diagnosis of Fibromyalgia Syndrome

# MOLECULAR NEUROBIOLOGY

Volume 54 • Number 9

November 2017



Fibromyalgia and Circulating microRNAs

© Springer Nicolas G. Bazan, Editor-in-Chief

ISSN: 0893-7648
eISSN: 1559-1182
12035 • 54(9) 6647-7554 (2017)

## ORIGINALRESEARCH doi:10.1111/ijpo.12133

Oral glucose tolerance test unravels circulating miRNAs associated with insulin resistance in obese preschoolers

A. Masotti,<sup>1†</sup> A. Baldassarre,<sup>1†</sup> M. Fabrizi,<sup>2</sup> G. Olivero,<sup>3</sup> M. C. Loreti,<sup>3</sup> P. Giammaria,<sup>3</sup> P. Veronelli,<sup>3</sup> M. P. Graziani<sup>3</sup> and M. Manco<sup>2</sup>

<sup>1</sup>Gene expression – Microarrays Laboratory, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy, <sup>2</sup>Research Unit for Multifactorial Disease, Scientific Directorate, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy, and <sup>3</sup>Federazione Italiana Medici Pediatri, FIMP, Rome, Italy

#### Summary

Background: Circulating microRNAs (miRNAs) may act as biomarkers of metabolic disturbances.

Objective: The aim of this study was to identify serum miRNAs signature of early insulin resistance in obese preschoolers.

ORIGINALRESEARCH

## Celiac disease and adherence to gluten-free diet

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau

(43) International Publication Date WIPO PCT 24 June 2021 (24.06.2021)

#### 

(10) International Publication Number WO 2021/124369 A1

- (51) International Patent Classification: C12Q 1/6883 (2018.01)
- (21) International Application Number:

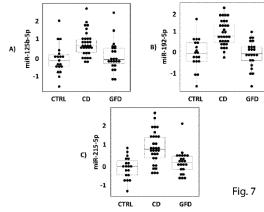
PCT/IT2020/050313

- (22) International Filing Date: 18 December 2020 (18.12.2020)
- (25) Filing Language:
- (26) Publication Language:
- (30) Priority Data:

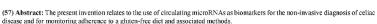
- 102019000024550 18 December 2019 (18.12.2019) IT
- (71) Applicant: OSPEDALE PEDIATRICO BAMBINO GESU' [IT/IT]; PIAZZA S.ONOFRIO, 4, 00165 ROMA (84) Designated States (unless otherwise indicated, for every
- (72) Inventors: MASOTTI, Andrea; c/o OSPEDALE PEDIA-TRICO BAMBINO GESU', PIAZZA S.ONOFRIO, 4. 00165 ROMA (IT). FELLI, Cristina: c/o OSPEDALE PEDIATRICO BAMBINO GESU', PIAZZA S.ONOFRIO, 4, 00165 Roma (RM) (IT).

- (74) Agent: GITTO, Serena et al.; c/o Barzano & Zanardo Roma S.p.A., Via Piemonte, 26, 00187 Rome (IT).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, IT, JO, JP, KE, KG, KH, KN KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, OA, RO, RS, RU, RW SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW
- kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ. UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW KM, ML, MR, NE, SN, TD, TG).

(54) Title: CIRCULATING MICRO-RNAS AS BIOMARKERS FOR THE DIAGNOSIS OF CELIAC DISEASE AND FOR MONI-TORING ADHERENCE TO A GLUTEN-FREE DIET



disease and for monitoring adherence to a gluten-free diet and associated methods.







### Circulating microRNAs as novel non-invasive biomarkers of paediatric celiac disease and adherence to gluten-free diet



Cristina Felli,<sup>a</sup> Antonella Baldassarre,<sup>a</sup> Paolo Uva,<sup>b</sup> Anna Alisi,<sup>a,c</sup> Davide Cangelosi,<sup>b</sup> Monica Ancinelli,<sup>d</sup> Mariangela Caruso,<sup>e</sup> Alessandro Paolini, Alessia Montano, Marco Silano, Olimpia Vincentini, Carlo Catassi, Elena Lionetti, Simona Gatti, Francesca Ferretti, a,c and Andrea Masotti a,\*

<sup>a</sup>Research Laboratories, Bambino Gesù Children's Hospital-IRCCS, Rome, Italy

<sup>b</sup>Clinical Bioinformatics Unit, IRCCS Istituto Giannina Gaslini, Genoa, Italy

'Research Unit of Molecular Genetics of Complex Phenotypes, Research Laboratories, Bambino Gesù Children's

<sup>d</sup>Hepato-Gastroenterology and Nutrition Department, Research Laboratories, Bambino Gesù Children's Hospital-IRCCS,

eDepartment of Maternal Infantile and Urological Sciences, SAPIENZA University of Rome, Rome, Italy

fUnit of Human Nutrition and Health, Department of Food Safety, Nutrition and Veterinary Public Health, Istituto Superiore di Sanità, Rome, Italy

<sup>9</sup>Department of Pediatrics, Polytechnic University of Marche, Ancona, Italy

Background Celiac Disease (CD) is a multifactorial autoimmune enteropathy (with a prevalence of approximately 1% worldwide) that exhibits a wide spectrum of clinical, serological and histological manifestations. For the diagnosis of paediatric CD, the gold standard is the combination of serological tests (with high TGA-IgA values greater than 10 times the upper limit of normal) and duodenal biopsy (with a positive TGA-IgA but low titer). Therefore, a diagnostic test that totally excludes an invasive approach has not been discovered so far and the discovery of novel biological markers would represent an undoubted advantage for the diagnosis of CD and prognostic evaluation. MicroRNAs (miRNAs), small non-coding RNAs (18-22 nucleotides) that regulate gene expression at post-transcriptional level and play important roles in many biological processes, represent a novel class of potential disease biomarkers. Their presence in biological fluids (i.e., serum, plasma, saliva, urine) provides the opportunity to employ circulating miRNAs as novel non-invasive biomarkers.

Methods In our prospective observational study, we examined the expression of circulating miRNAs in a cohort of CD patients (both at diagnosis and on gluten-free diet, respectively referred as CD and GFD) compared to healthy controls. By small RNA-Seq we discovered a set of circulating miRNAs that were further validated by qPCR with specific assays.

Findings We found that out of the 13 miRNAs able to discriminate the three groups (i.e., CD, GFD and controls), three of them, namely miR-192-5p, miR-215-5p and miR-125b-5p (alone or in combination), were able to discriminate these three groups with high accuracy and specificity.

Interpretation Our conclusions emphasize that these circulating miRNAs can be employed not only for the diagnosis of CD patients with a low TGA-IgA titer but also to monitor the adherence to a gluten-free diet by CD patients. In conclusion, we suggest the use of the circulating miRNAs identified in this work as a novel diagnostic and follow-up tool

Funding This work was supported by Fondazione Celiachia Onlus (FC) Grant n° 018/FC/2013 and by Italian Ministry of Health (Ricerca Corrente).

Copyright © 2022 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/)

#### Introduction

Celiac Disease (CD) is an autoimmune enteropathy distributed worldwide with a prevalence of approximately 1%. Teliac disease is multifactorial and exhibits a wide

eBioMedicine 2022;76: Published online xxx https://doi.org/10.1016/j. ebiom.2022.103851

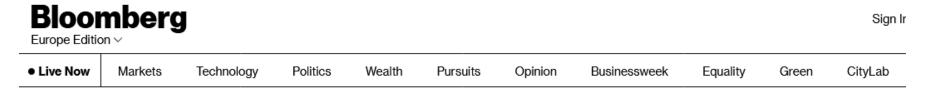
> THE LANCET EBioMedicine. 2022, 76:103851.

\*Corresponding author. E-mail address: andrea.masotti@opbg.net (A. Masotti).

WO2021124369A1

www.thelancet.com Vol 76 Month , 2022

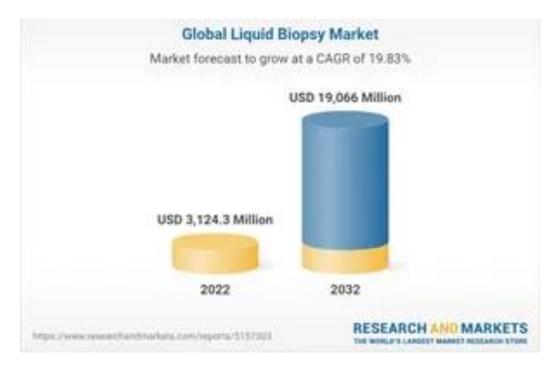
## The Market of Liquid Biopsies



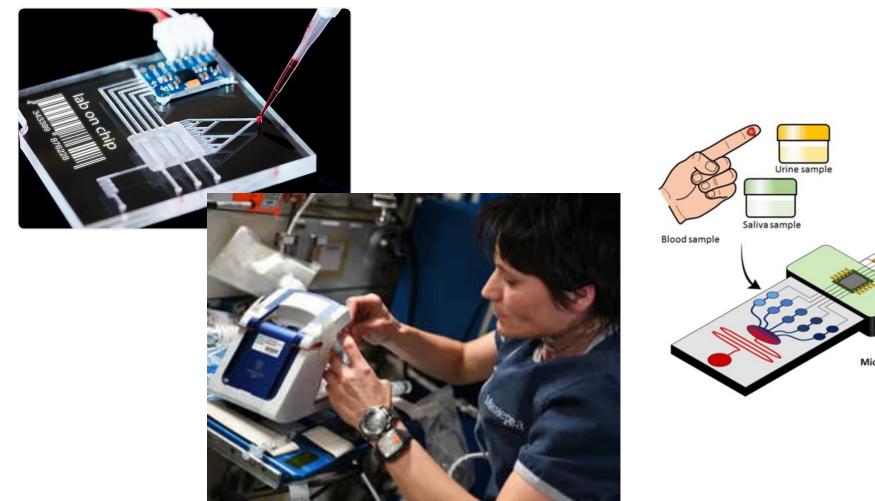
#### **Business**

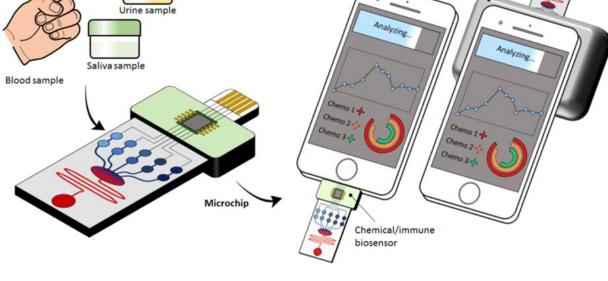
# BIS Research Study Highlights the Global Liquid Biopsy Market to Reach \$19.06 Billion by 2032





## **Perspectives**





Smartphone

Optical sensing

The astronaut Samantha Cristoforetti collects a single biological sample, which could be blood, saliva or urine, on a nanostrip. The strip is inserted into the device. (Image Source: NASA)

## **Opportunities**

Validation of the diagnostic test on 1200 patients → Funds (public)
Assessing the methodology using different biological fluids (i.e., urine, feces, sweat, tears)

## **Development of:**

- a commercial IVD kit
- a kit for other techniques (i.e. cytofluorimetry)
- a kit for portable qPCR machine →

Funds
Licencing

**Industrial partnership** 

Prototyping (i.e., microfluidic/miniaturization) → Industrial partnership
 Funds



# Thank you for your attention

## **Andrea Masotti PhD**

San Paolo Research Laboratories, Bambino Gesù Children's Hospital-IRCCS Viale di San Paolo 15, 00146 Rome Italy

tel: +39-06-6859-2650

email: andrea.masotti@opbg.net

https://www.ospedalebambinogesu.it/

https://www.tentacles-enm3.eu/

## Andrea Masotti's Group



Andrea Masotti (PI)

Antonella Baldassarre

(Post-Doc)



Alessandro Paolini (Post-Doc)



Elena Cheri (Post-graduate)



Cristina Felli (Collaborator)



Stefania Paola Bruno (Doctoral fellow)





Meysam Sarsharjeryandeh (Post-Doc)